

=> gene (s) gun  
L1 1466 GENE (S) GUN

=> HSV and L1  
L2 5 HSV AND L1

=> vector and L1  
L3 445 VECTOR AND L1

=> "25 kilobase"  
L4 297 "25 KILOBASE"

=> L1 and L4  
L5 0 L1 AND L4

=> "5 kilobase"  
L6 3997 "5 KILOBASE"

=> L1 and L6  
L7 0 L1 AND L6

=> HIV and L1  
L8 70 HIV AND L1

=> adenovirus and l1  
L9 41 ADENOVIRUS AND L1

=> "viral vector"  
L10 13167 "VIRAL VECTOR"

=> L10 and L8  
L11 8 L10 AND L8

=> L10 and L9  
L12 13 L10 AND L9

=> HBV and L10  
L13 44 HBV AND L10

=> L13 and l1.  
L14 0 L13 AND L1

=> HBV and l1  
L15 14 HBV AND L1

=> PHV and L10  
L16 0 PHV AND L10

=> DNA (w) vaccine  
L17 6153 DNA (W) VACCINE

=> L1 and L17  
L18 407 L1 AND L17

=> HCV and L18  
L19 3 HCV AND L18

=> HBV and L18  
L20 5 HBV AND L18

=> HIV and L17  
L21 780 HIV AND L17

=> L1 and L21  
L22 27 L1 AND L21

=> cosmid

*Updated search  
06/08/2005  
BGLi*

L23 12065 COSMID

=> L23 and L17

L24 3 L23 AND L17

=> L23 and L1

L25 4 L23 AND L1

=> gold and l1

L26 200 GOLD AND L1

=> L26 and L15

L27 1 L26 AND L15

=> L26 and L12

L28 0 L26 AND L12

=> L26 and L11

L29 5 L26 AND L11

=> L26 and L2

L30 0 L26 AND L2

=> L26 and L19

L31 0 L26 AND L19

=> L26 and L20

L32 0 L26 AND L20

=> L26 and L22

L33 1 L26 AND L22

=> L26 and L24

L34 0 L26 AND L24

=> L26 and L25

L35 0 L26 AND L25

=> D L27 IBIB ABS

ACCESSION NUMBER: 1998:788681 CAPLUS

DOCUMENT NUMBER: 130:51331

TITLE: Preparation and use of **viral vectors**  
for mixed envelope protein immunogenic composition  
against human immunodeficiency viruses

INVENTOR(S): Hurwitz, Julia; Slobod, Karen

PATENT ASSIGNEE(S): St. Jude Children's Research Hospital, USA

SOURCE: U.S., 36 pp., Cont.-in-part of U.S. 5,741,492.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5846546	A	19981208	US 1997-788815	19970123
US 5741492	A	19980421	US 1996-590288	19960123
CA 2243570	AA	19970731	CA 1997-2243570	19970123
CA 2243570	C	20010814		
CN 1214083	A	19990414	CN 1997-193234	19970123
EP 1378516	A1	20040107	EP 2003-77363	19970123

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
IE, SI, LT, LV, FI, RO, AL

US 6086891 A 20000711 US 1998-157963 19980921

US 6723558 B1 20040420 US 2000-568105 20000510

PRIORITY APPLN. INFO.:

US 1996-590288 A2 19960123

US 1997-788815 A3 19970123

EP 1997-903823 A3 19970731

US 1998-157963 A1 19980921

AB Polyenv immunogenic composition are provided that comprise mixts. of at least 4 different recombinant viruses that each express a different **HIV** env variant or a portion thereof containing both constant and variable regions, as well as methods of making and using such polyenv immunogenic composition and viruses. The immunogenic composition of the invention are optimally combined with a recombinant **HIV** env booster, or a recombinant **HIV** env gene DNA priming or boosting vaccine.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ACCESSION NUMBER: 1997:305212 CAPLUS

DOCUMENT NUMBER: 126:338815

TITLE: Topical application of viral vectors for epidermal gene transfer

AUTHOR(S): Lu, Bo; Federoff, Howard J.; Wang, Yibin; Goldsmith, Lowell A.; Scott, Glynis

CORPORATE SOURCE: Departments Dermatol. Neurol., Univ. Rochester Sch. Med. Dentistry, Rochester, NY, USA

SOURCE: Journal of Investigative Dermatology (1997), 108(5), 803-808

CODEN: JIDEAE; ISSN: 0022-202X

PUBLISHER: Blackwell

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Efficient gene transfer with extended gene expression is essential for successful treatment of skin diseases using gene therapy. Previously we evaluated a phys. **gene** transfer method (**gene gun** delivery) for its ability to transfer the epidermis in vivo. In this study, we tested two viral vectors for their ability to transduce murine epidermis through topical application. Both an adenoviral vector and a herpes simplex virus (**HSV**) amplicon vector transduced murine epidermis with high efficiency after topical application. Differences in amount and duration of transgene expression were compared between these two vectors. Quant. anal. of reporter lacZ **gene** expression showed that the viral vector-mediated **gene** transfers were superior to **gene-gun** delivery of plasmid DNA. Significant necrosis and cytotoxicity, however, were observed in the **HSV**-treated skin. In addition, we show that murine epidermis developed hyperkeratosis and acanthosis 4 d after an adenoviral vector containing a human TGF- $\alpha$  expression unit was applied topically. Finally we demonstrate the feasibility of transduction of fetal skin in utero by intraamniotic injection of an adenovirus vector.

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ACCESSION NUMBER: 1997:454559 BIOSIS  
DOCUMENT NUMBER: PREV199799753762  
TITLE: Manipulation of **HIV-1** gp120-specific immune  
responses elicited via **gene gun**-based  
DNA immunization.  
AUTHOR(S): Prayaga, Sudhirdas K.; Ford, Maura J.; Haynes, Joel R.  
[Reprint author]  
CORPORATE SOURCE: Heska Corp., 1825 Sharp Point Dr., Fort Collins, CO 80525,  
USA  
SOURCE: Vaccine, (1997) Vol. 15, No. 12-13, pp. 1349-1352.  
CODEN: VACCDE. ISSN: 0264-410X.  
DOCUMENT TYPE: Article  
LANGUAGE: English  
ENTRY DATE: Entered STN: 27 Oct 1997  
Last Updated on STN: 27 Oct 1997

AB **Gene gun**-based DNA immunization using vectors encoding  
**HIV-1** gp120 or influenza virus nucleoprotein result in Th2-like  
immune responses following successive immunizations. The codelivery of  
vectors encoding IL-2, IL-7, or IL-12 blocked this effect by markedly  
enhancing gp120-specific interferon gamma production, and suppressing IL-4  
and IgG1 responses. An unbiased augmentation of all immune responses was  
observed by increasing the resting period between immunizations. In this  
case, IFN-gamma production following in vitro stimulation increased by  
over 1000-fold, while IL-4, IgG1, and IgG2a responses were elevated as  
well. Interestingly, cytokine gene codelivery, in the context of the  
longer resting period, provided no additional stimulation of Th1-like  
responses such as IFN-gamma and IgG2a production, although there was still  
some suppression of IL-4 production. These data demonstrate that the  
quality and magnitude of responses elicited following epidermal  
administration of **DNA vaccines** can be manipulated by  
multiple means.

ACCESSION NUMBER: 1997:366986 BIOSIS  
DOCUMENT NUMBER: PREV199799658919  
TITLE: Enhancement of immunodeficiency virus-specific immune  
responses in DNA-immunized rhesus macaques.  
AUTHOR(S): Fuller, Deborah H. [Reprint author]; Corb, Michael Murphey;  
Barnett, Susan; Steimer, Kathelyn; Haynes, Joel R. [Reprint  
author]  
CORPORATE SOURCE: Auragen Inc., Middleton, WI, USA  
SOURCE: Vaccine, (1997) Vol. 15, No. 8, pp. 924-926.  
CODEN: VACCDE. ISSN: 0264-410X.  
DOCUMENT TYPE: Article  
LANGUAGE: English  
ENTRY DATE: Entered STN: 25 Aug 1997  
Last Updated on STN: 25 Aug 1997

AB In contrast to results obtained with plasmid DNA vectors encoding antigens  
from viruses such as influenza and hepatitis B, plasmids coding for  
antigens from primate immunodeficiency viruses have elicited relatively  
weak antibody responses following **gene gun**-mediated  
DNA immunization of rhesus monkeys. In an effort to augment these  
responses, the importance of the immunization schedule was investigated,  
as well as the possible synergy that might result from boosting  
**gene gun**-primed animals with other routes of  
immunization. Here we demonstrate that endpoint gp120-specific antibody  
titers can be enhanced as much as tenfold by reducing the number of  
immunizations and lengthening the resting period between immunizations.  
In addition, boosting **gene gun**-primed animals with  
either recombinant subunits or gp120-expressing vaccinia recombinants  
resulted in synergistic responses.

TITLE: Immune responses but no protection against SHIV by **gene-gun** delivery of **HIV-1** DNA followed by recombinant subunit protein boosts.

AUTHOR(S): Putkonen, Per [Reprint author]; Quesada-Rolander, Marlene; Leandersson, Ann-Charlotte; Schwartz, Stefan; Thorstensson, Rigmor; Okuda, Kenji; Wahren, Britta; Hinkula, Jorma

CORPORATE SOURCE: Swedish Inst. Infectious Dis. Control, Microbiol Tumoriol Cent., Karolinska Inst., S-105 21 Stockholm, Sweden

SOURCE: Virology, (Oct. 25, 1998) Vol. 250, No. 2, pp. 293-301. print.  
CODEN: VIRLAX. ISSN: 0042-6822.

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 18 Dec 1998  
Last Updated on STN: 18 Dec 1998

AB The efficacy of combining immunization with human immunodeficiency virus type 1 (**HIV-1**) DNA and **HIV-1** recombinant proteins to obtain protection from chimeric simian/human immunodeficiency virus (SHIV) was determined. Four cynomolgus monkeys received four **gene-gun** immunizations intraepidermally of plasmid DNA encoding **HIV-1** LAI env (gp160), gag, tat, nef, and rev proteins. Ten micrograms of DNA was used per immunization. The animals were boosted twice intramuscularly with 50 mug of **HIV-1**LAI Env (MicroGeneSys), Gag, Tat, Nef, and Rev recombinant proteins mixed in Ribi adjuvant. The antibody responses were amplified following the administration of the recombinant subunit boosts. One month after the final subunit immunization, the vaccinated animals-together with four control animals were challenged intravenously with 10 monkey infectious doses of SHIV that expresses the env, tat and rev genes of **HIV-1** and gag and nef from SIV. However, only low titers of neutralizing antibodies were present at the day of challenge. The consecutive **HIV-1** DNA and recombinant protein immunizations induced B- and T-cell responses but not protection against SHIV replication nor reduction of the viral load.

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ACCESSION NUMBER: 1998:257620 BIOSIS

DOCUMENT NUMBER: PREV199800257620

TITLE: Improved humoral and cellular immune responses against the gp120 V3 loop of **HIV-1** following genetic immunization with a chimeric **DNA vaccine** encoding the V3 inserted into the hepatitis B surface antigen.

AUTHOR(S): Fomsgaard, A., H. V. Nielsen [Reprint author]; Bryder, K.; Nielsen, C.; Machuca, R.; Bruun, L.; Hansen, J.; Buus, S.

CORPORATE SOURCE: Dep. Virol., Statens Serum Inst., 5 Artillerivej DK-2300 Copenhagen S, Denmark

SOURCE: Scandinavian Journal of Immunology, (April, 1998) Vol. 47, No. 4, pp. 289-295. print.  
CODEN: SJIMAX. ISSN: 0300-9475.

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 9 Jun 1998  
Last Updated on STN: 9 Jun 1998

AB The gp120-derived V3 loop of **HIV-1** is involved in co-receptor interaction, it guides cell tropism, and contains an epitope for antibody neutralization. Thus, **HIV-1** V3 is an attractive vaccine candidate. The V3 of the MN strain (MN V3) contains both B- and T-cell epitopes, including a known mouse H-2d-restricted cytotoxic T lymphocyte (CTL) epitope. In an attempt to improve the immunogenicity of V3 in **DNA vaccines**, a plasmid expressing MN V3 as a fusion protein with the highly immunogenic middle (pre-S2+S) surface antigen of hepatitis B virus (HBsAg) was constructed. Epidermal inoculation by **gene gun** was used for genetic immunization in a mouse model. Antibody and CTL responses to MN V3 and HBsAg were measured and compared with the immune responses obtained after vaccination with plasmids encoding the complete **HIV-1** MN gp160 and HBsAg

(pre-S2+S), respectively. DNA vaccination with the **HIV** MN gp160 envelope plasmid induced a slow and low titred anti-MN V3 antibody response at 12 weeks post-inoculation (p.i.) and a late appearing (7 weeks), weak and variable CTL response. In contrast, DNA vaccination with the HBsAg-encoding plasmid induced a rapid and high titred anti-HBsAg antibody response and a uniform strong anti-HBs CTL response already 1 week p.i. in all mice. DNA vaccination with the chimeric MN V3/HBsAg plasmid elicited humoral responses against both viruses within 3-6 weeks which peaked at 6-12 weeks and remained stable for at least 25 weeks. In addition, specific CTL responses were induced in all mice against both MN V3 and HBsAg already within the first 3 weeks, lasting at least 11 weeks. Thus, HBsAg acts as a 'genetic vaccine adjuvant' augmenting and accelerating the cellular and humoral immune response against the inserted MN V3 loop. Such chimeric **HIV**-HBsAg plasmid constructs may be useful in DNA immunizations as a 'carrier' of protein regions or minimal epitopes which are less exposed or poorly immunogenic.

ACCESSION NUMBER: 1999:195880 BIOSIS  
DOCUMENT NUMBER: PREV199900195880  
TITLE: **HIV-1 DNA vaccines.**  
AUTHOR(S): Fomsgaard, Anders [Reprint author]  
CORPORATE SOURCE: Department of Virology, Statens Serum Institut, 5  
Artillerivej, DK-2300, Copenhagen S, Denmark  
SOURCE: Immunology Letters, (Jan., 1999) Vol. 65, No. 1-2, pp.  
127-131. print.  
CODEN: IMLED6.. ISSN: 0165-2478.  
DOCUMENT TYPE: Article  
LANGUAGE: English  
ENTRY DATE: Entered STN: 25 May 1999  
Last Updated on STN: 25 May 1999

AB **HIV-1** was among the original **DNA vaccine** targets and **HIV DNA vaccines** are now in human trials. Lack of strong correlates of protective immunity makes vaccine design difficult; however, **DNA vaccines** have the potential to be an ideal vaccine and therapeutic approach against **HIV-1**. **DNA vaccines** induce conformational -dependent antibodies, mimic live vaccines but without the pathogenic potential, and can easily be made polyvalent. Genes which encode important CTL and antibody epitopes can be included while those that confer pathogenicity, virulence, antibody enhancement or represent non-conserved epitopes can be excluded. In our hands pre-treatment of muscles with bupivacaine or cardiotoxin did not offer any advantage over no muscle pre-treatment or **gene gun** inoculation of skin although **gene gun** immunization seem to favour a Th2 type response. As **DNA vaccine** candidates we have compared vaccines encoding native **HIV** MN gp160 with Rev-independent synthetic genes encoding MNgp160 and MNgp120 using mammalian high expression codons. In these experiments the gene encoding secreted gp120 gave highest antibody neutralizing titers. High and fast antibody responses could also be obtained by transferring the **HIV** -1 MN V3 loop to the secreted HBsAg as a fusion gene vaccine. Thus, in the case of **HIV-1** MN genes encoding secreted surface glycoproteins may be preferred instead of membrane bound envelopes. CTL responses were induced in all cases. However, in order to meet the high diversity of **HIV** and HLA types our approach is to include many CTL epitopes in a multivalent minigene vaccine. We found that **gene gun** DNA vaccination with minimal epitopes could induce specific CTL. Flanking sequences influenced the CTL response but was not needed. **DNA vaccines** encoding known and computer predicted CTL epitopes are now being developed.



ACCESSION NUMBER: 1999:216837 BIOSIS  
DOCUMENT NUMBER: PREV199900216837  
TITLE: Induction of mucosal IgA by a novel jet delivery technique  
for **HIV-1** DNA.  
AUTHOR(S): Lundholm, Peter [Reprint author]; Asakura, Yusuke; Hinkula,  
Jorma; Lucht, Erik; Wahren, Britta  
CORPORATE SOURCE: Swedish Institute for Infectious Disease Control,  
Microbiology and Tumorbiology Center, Karolinska Institute,  
171 82, Stockholm, Sweden  
SOURCE: Vaccine, (April 9, 1999) Vol. 17, No. 15-16, pp. 2036-2042.  
print.  
CODEN: VACCDE. ISSN: 0264-410X.  
DOCUMENT TYPE: Article  
LANGUAGE: English  
ENTRY DATE: Entered STN: 26 May 1999  
Last Updated on STN: 26 May 1999

AB Novel ways of delivering plasmid DNA to elicit humoral IgA, IgG and  
cell-mediated immune responses in mice were investigated. Intraoral  
administration of DNA in the cheek, using a jet immunization technique,  
elicited the highest IgA mucosal responses. Intranasal immunization gave  
strong mucosal IgA responses and persistent systemic IgG. Immunoglobulin  
isotype analysis revealed an IgG1 profile for intramuscular tongue and  
**gene gun** immunizations and an IgG2a profile following  
oral jet injection and intranasal application. The route of delivery was  
of importance for the characteristics and quality of the mucosal immune  
response following DNA immunization. For **DNA vaccine**  
delivery, the intraoral jet injection technique has the advantages of  
being a simple and rapid way of administering the DNA in solution and of  
provoking specific mucosal IgA when administered in the mucosal associated  
lymphoid tissue.

ACCESSION NUMBER: 1998:426180 CAPLUS  
DOCUMENT NUMBER: 129:201753  
TITLE: **DNA vaccines**: a review of developments  
AUTHOR(S): Webster, Robert G.; Robinson, Harriet L.  
CORPORATE SOURCE: Department of Virology and Molecular Biology, St. Jude Children's Research Hospital, Memphis, TN, USA  
SOURCE: BioDrugs (1997), 8(4), 273-292  
CODEN: BIDRF4; ISSN: 1173-8804  
PUBLISHER: Adis International Ltd.  
DOCUMENT TYPE: Journal; General Review  
LANGUAGE: English

AB A review with 110 refs. Immunization with purified DNA is a powerful technique for inducing immune responses. The concept is very simple, involving insertion of the gene encoding the antigen of choice into a bacterial plasmid, and injection of the plasmid into the host where the antigen is expressed and induces humoral and cellular immunity. This technol. can induce immunity to all antigens that can be encoded by DNA; this includes all protein, but not carbohydrate, antigens. DNA immunization appears to result in presentation of antigens to the host's immune system in a natural form, similar to that achieved with live attenuated vaccines. The most efficacious routes for DNA immunization are bombardment with particles coated with DNA (**gene-gun**), followed by i.m. and intradermal administration. The efficiency of transfection of host cells is low, but sufficient to induce immunol. responsiveness. The DNA plasmid is retained in the transfected cells in an unintegrated form for the life of the cell. The majority of transfected cells are eliminated, but residual expression has been detected for longer periods. In animal model systems, DNA immunization has been shown to induce protective immunity to influenza, herpes, rabies, hepatitis B and lymphocytic choriomeningitis viruses, and to malaria and mycobacteria. However, strategies to induce protective immunity to **HIV** and other disease agents remain to be developed. **DNA vaccines** permit modulation of the immune response by altering the route or method of DNA administration, by including immunostimulatory sequences in the plasmid, and by co-administration of cytokine genes with the gene encoding the antigen of interest. A T helper 1 response provides cell-mediated immune killing of infected cells and neutralizing antibody production, while a T helper 2 response induces IgE and allergic responses. The advantages of DNA immunization are: (i) similarity to live attenuated vaccination but without the possibility of contamination with undesirable agents; (ii) correct presentation of antigen; (iii) combinations of DNA-encoded antigens and/or cytokines may be administered; (i.v.) genetic stability; (v) potential speed of making new vaccines with genetic identity; (vi) development of vaccines for agents that cannot be grown in culture; (vii) no need for a cold chain; and (viii) possibility of modulation of the immune response. The perceived risks include: (i) integration of the plasmid into the host genome; (ii) induction of anti-DNA antibodies and autoimmunity; and (iii) induction of tolerance. The available information concerning safety is encouraging, with the risk of integration being considered to be orders of magnitude below the spontaneous mutation frequency in humans. DNA immunization offers the possibility of extending the control of infectious diseases far beyond those that are currently controlled by conventional and recombinant vaccines, to include vaccines for parasites and cancer. However, it is currently too early to predict the future extent of use of **DNA vaccines** in human immunization programs because the initial clin. trials are still in progress.

ACCESSION NUMBER: 1999:204105 BIOSIS  
DOCUMENT NUMBER: PREV199900204105  
TITLE: Improved immunogenicity of HIV-1 epitopes in HBsAg chimeric  
DNA vaccine plasmids by structural mutations of HBsAg.  
AUTHOR(S): Bryder, Karin; Sbai, Hakima; Nielsen, Henrik V.; Corbet,  
Sylvie; Nielsen, Claus; Whalen, Robert G.; Fomsgaard,  
Anders [Reprint author]  
CORPORATE SOURCE: Molecular Biology Laboratory, Department of Virology,  
Statens Serum Institut, 5 Artillerivej, DK-2300, Copenhagen  
S, Denmark  
SOURCE: DNA and Cell Biology, (March, 1999) Vol. 18, No. 3, pp.  
219-225. print.  
CODEN: DCEBE8. ISSN: 1044-5498.  
DOCUMENT TYPE: Article  
LANGUAGE: English  
ENTRY DATE: Entered STN: 26 May 1999  
Last Updated on STN: 26 May 1999

AB To improve the immunogenicity of epitopes from the envelope protein of  
HIV-1, we have developed **gene gun**-delivered subunit  
DNA vaccines by inserting the sequences encoding the V3 region into the  
hepatitis B virus (HBV) envelope **gene**, often called  
the surface antigen (HBsAg). We have examined the possibility of  
modifying the immune response to V3 by introducing modifications into the  
carrier HBsAg in **gene gun** DNA immunization of mice.  
In some plasmid constructions, the V3 sequence was introduced into the  
preS2 region of the HBsAg. Although this region is not present in all  
protein subunits of the HBsAg particles produced, abolishing the internal  
translational initiation site for the S protein had no effect on the  
immune response to V3. Expression of V3 at the N-terminal or C-terminal  
part of the HBsAg protein resulted in equal anti-V3 antibody and cytotoxic  
T-lymphocyte (CTL) responses. However, elimination of secretion by single  
amino-acid mutations in the HBsAg decreased the anti-HBsAg antibody  
response but enhanced the anti-V3 antibody response. In contrast, the CTL  
response to V3 was independent of the structural mutations but could be  
improved by a total deletion of the HBsAg sequence part. Thus, the immune  
response to heterologous epitopes can be altered by modifications in the  
carrier HBsAg protein. Modifications of the HBsAg carrier might interfere  
with the dominant immune response to the HBsAg epitopes, allowing better  
antibody induction to less immunogenic foreign epitopes. However, for  
induction of CTL responses, the expression of minimal epitopes may be  
advantageous.